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EFFECTS OF MILD UPPER RESPIRATORY TRACT ILLNESSES ON MOOD AND COGNITION

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ABSTRACT

Background: The aetiology and pathogenesis of mild upper respiratory tract illnesses (MURTIs) are well-documented. These illnesses lead to malaise, which reflects reduced well-being, fatigue and impaired performance. This was examined in the present study. **Methods:** Sixty volunteers participated in the study. Twenty-one of these had a MURTI at the first test session. They returned for a second test session when they were healthy. They were compared with thirty-nine participants who were healthy on both occasions. Mood rating and cognitive performance tasks were carried out in each test session, and a symptom checklist was completed. **Results**: The first analyses compared those with MURTIs with the healthy group. The MURTI group were less alert and had slower reaction times in simple and choice reaction time tasks. They detected fewer targets in a sustained attention task and were less accurate on a verbal reasoning task. Specific comparisons were then made between the healthy (N=39), sore throat (N=6), cough (N=3), and headache (N=6) groups. All symptom groups were less alert than the healthy group. The headache group showed the greatest impairments with reduced recall of a list of words and attention problems. **Conclusion:** Individuals with a MURTI were less alert and had a more negative mood than those who were healthy. They also responded more slowly on simple and choice reaction time tasks, had impaired sustained attention, and had less accurate verbal reasoning. Analysis of the specific symptom groups confirmed that having a headache was associated with the greatest impairment. Future research must now examine whether therapies can remove the malaise associated with MURTIs.

KEYWORDS: Mild upper respiratory tract illnesses (MURTIs); Cough; Sore throat; Headache; Reaction time; Alertness; Cognition; Hedonic tone.

INTRODUCTION

There is now a detailed knowledge of the aetiology and pathogenesis of mild upper respiratory tract illnesses (MURTIs). Details are given in three review articles.[1-3] The main points can be briefly summarised as follows. MURTIs are caused by infections with viruses such as rhinoviruses and coronaviruses. The large number of infecting agents makes it difficult to prevent them by vaccination, although this can be applied to influenza. The viral infection of the nasal cells leads to different symptoms, the main ones being nasal congestion, a runny nose, a cough, and a sore throat. The pathways leading to these symptoms and key mediators are shown below:

- Sensitisation of airway receptors, cholinergic stimulation, and bronchoconstriction leads to cough. This reflects changes in the medulla region of the brain stem triggered by stimulation in the respiratory tract.
- Sneezing and a sore throat reflect the infection of the nasal cells. This leads to stimulation of the sneeze centre in the brainstem. Histamine generates sneezing, and a sore throat reflects the action of bradykinins and prostaglandins.
- Nasal congestion is due to increased inflammation, vasodilation and tissue edema. A blocked nose reflects congestion of nasal blood vessels. Sympathetic nerves produce noradrenaline to reduce swelling.
- A runny nose reflects increased mucus production, increased vascular permeability and serum transudation. A reflex action of the parasympathetic nerves increases glandular secretion.

Other symptoms, such as fever (due to cytokine action) and myalgia (due to TNF leading to a breakdown of skeletal muscle), may occur, and these are more common in influenza than the common cold. Another general symptom is known as malaise, which reflects the increased fatigue and reduction of well-being induced by MURTIs. MURTIS are widespread, frequent and a major cause of absenteeism from education and work. In

addition to absenteeism, epidemiological studies have shown that MURTIs may reduce work productivity, efficiency and academic attainment.[4-7]

Research has demonstrated that MURTIs reduce well-being and can impair the efficiency of mental functioning. Initial evidence for such effects came largely from anecdotal reports and case histories.[8,9] Studies of experimentally induced illnesses have confirmed that such illnesses produce behavioural changes. This research started with the study of severe illnesses which had global effects on behaviour.[9-13] Several reviews discuss research on both effects of experimentally induced MURTIs and naturally-occurring illnesses.[14-18]

The research on experimentally induced MURTIs showed that both colds and influenza have selective effects on mental functioning, with only some aspects of performance being impaired.[19-30] The profile of impairments has been found to be different in studies of influenza from those observed in experiments on the effects of colds. Influenza impaired detection of stimuli presented at uncertain times or unknown locations. However, neither motor performance nor higher cognitive functions appear to be affected by influenza. In contrast, the common cold 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.

The effects of influenza have been replicated in a study of naturally occurring illnesses that involve virological techniques to identify the infecting agent.[31] Similarly, studies of naturally occurring colds have confirmed that such illnesses reduce alertness and lead to psychomotor slowing.[32-42] Other research has looked at the effects of other factors which change alertness in those with a MURTI and those who are healthy.[43-49] Factors such as stress, fatigue and alcohol had a greater effect on those with a MURTI. Stimulants, such as caffeine, removed many of the impairments induced by the MURTI.

Other research has examined simulations of real-life activities such as driving.[50,51] These studies also demonstrated MURTI-induced impairments, confirming results from the earlier research. Other research.[52] has examined the effects of headaches on mental functioning. Results from this study suggest that different aspects of memory (working memory, retrieval from semantic memory) are also impaired when individuals are suffering from a headache.

There were two main aims of the present research. The first aim was to extend research on minor illnesses and performance to cover a wider range of symptoms. Headache, sore throat, and cough were examined. A second aim was to use a wide selection of cognitive tasks to provide a more detailed profile of the effects of MURTIs on cognitive functions.

METHOD

Ethical approval and informed consent

The study was carried out with the approval of the Ethics Committee, School of Psychology, Cardiff University. 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.

Experimental design

A between-groups design was employed. Volunteers contacted the Centre when they were experiencing an acute illness. Participants were familiarised with the testing procedures and practised the tasks. Symptom severity of the illness was measured, and a battery of mood and performance tasks was then administered. This procedure was repeated when the volunteer was healthy, seven days after recovering fully from the illness. A cohort of healthy controls was also recruited (i.e., volunteers who had experienced no symptoms of an illness for one week). These healthy controls were tested twice, the second test being a week after the first, and the participants were healthy on both occasions. The healthy controls were matched as far as possible with the acute illness group in terms of time of testing (a.m. / p.m.) and gender (see Figure 1).

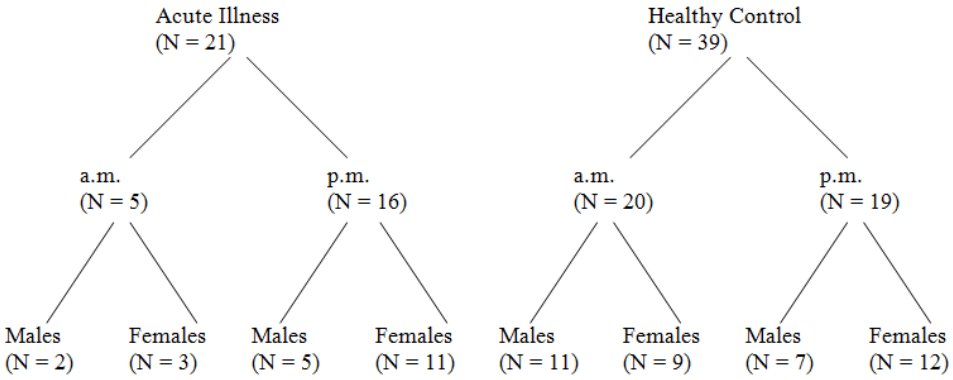

Figure 1: Experimental Groupings.

Participants

Sixty students (25 male and 35 female) were recruited from the volunteer panel of the Centre for Occupational and Health Psychology at Cardiff University. Participants were paid £15.00 on completion of the study.

Exclusion criteria

Several exclusion criteria were applied for the recruitment of participants in this investigation.

- Participants were not taking any medication (excluding the oral contraceptive pill or Ventolin).
- Volunteers were required to be students aged between eighteen and thirty years who smoked less than five cigarettes in the daytime and consumed less than twenty units of alcohol during the week.
- To be included in the study, participants must not have been involved in another study or drug investigation within the previous four weeks.

Additional requirements for participants in the acute illness condition were that they must be experiencing an acute illness and score a minimum of ***'5'*** on the symptom severity scales.

For the second test session for the acute illness group and for both baseline and test sessions for the healthy control group, participants were required to be in good general health (not experienced an acute illness for a week prior to the test session). In addition, a maximum total symptom score of ***'4'*** had to be recorded on the symptom severity scales, with a maximum rating of 1 on any individual symptom.

Schedule of testing

Participants suffering from an acute illness were tested as soon as possible after the onset of symptoms and reporting the illness to the Centre. Prior to all other test sessions, participants were required to be in good general health for a minimum period of one week. Several test day prerequisites were enforced to eliminate possible factors influencing performance. All participants were required not to have taken any medication for 24 hours prior to each test session. On the evenings prior to each test session, participants were required to limit their alcohol consumption to a maximum of four units and abstain from alcohol on these test days. Smoking and consumption of caffeinated products were prohibited two hours prior to the test sessions. Participation in vigorous exercise was also prohibited on these test days. Test sessions were carried out either A.M. or P.M., and this was consistent across the test sessions. The schedule of events for both test sessions was as follows:

Table 1: Test day schedules.

Time	*Activity*
00 min	**Register** Check inclusion criteria, complete informed consent, check pre-assessment criteria, and complete the acute illness questionnaire.
10 mins	**Familiarisation session** Record body weight and sub-lingual temperature, short test battery
35 mins	Complete psychosocial questionnaires.
50 mins	**Testing session 1**
	Pre-performance oral temperature
	Complete pre-performance pain questionnaire
	Complete the pre-performance symptoms checklist.
	Complete the sleeping and eating questionnaire.
60 mins	Complete a battery of performance tests.
105 mins	Post-performance oral temperature
	Complete post-performance pain questionnaire
	Complete the post-performance symptoms checklist.
110 mins	End
	Testing session 2
00 mins	Check pre-assessment criteria
	Complete the psychosocial questionnaire.
15 mins	Pre-performance oral temperature
	Complete pre-performance pain questionnaire
	Complete the pre-performance symptoms checklist.
	Complete the sleeping and eating questionnaire.
25 mins	Complete a battery of performance tests.
70 mins	Post-performance oral temperature
	Complete post-performance pain questionnaire
	Complete the post-performance symptoms checklist.
75 mins	End

Those participants in the acute illness condition completed an acute illness questionnaire on arrival at the testing facility. This questionnaire ascertained the specific details of the illness along with the duration, location, and severity of pain. Any medications taken were also recorded in this questionnaire.

At each test session, participants completed a pain questionnaire, both pre and post-performance, which assessed the type and severity of pain experienced. These were rated on a ten-point scale with 0 = no pain and 10 = as much pain as I can stand.

Volunteers also completed a symptom checklist, both pre-and post-performance, which assessed the presence and severity of common symptoms associated with a wide range of acute illnesses (e.g., sore throat, headache, cough, nausea, etc.). These were rated on a five-point scale from 0 = not present to 4 = very severe. Pre- and post-performance sub-lingual temperature was also recorded. On each test day, participants also completed a sleeping and eating log to record sleep duration and quality, food consumption and intake of alcoholic drinks. Participants also completed several psychosocial questionnaire booklets. On completion of the first test session, participants were provided with an information sheet reminding them of the test day requirements necessary for the second test session.

Measures

Visual analogue mood scales

Mood was assessed both pre- and post-performance using 18 computerised visual analogue mood rating scales. Each of the 18 bipolar scales comprised a pair of adjectives, for instance, drowsy - alert or happy - sad. Participants were instructed to move the cursor from a central position anywhere along the horizontal rule, towards either end of the scale, until the cursor was at a position representative of their mood state at that exact time. These 18 scales were presented successively. Three main factors were derived from these scales: alertness, hedonic tone and anxiety.

Performance tasks

Performance was assessed on a range of cognitive tasks. All of the performance tasks outlined below were completed on each visit to the testing facility. The tasks were presented in a fixed order, as shown below. Each test session extended over a period of approximately 45 minutes.

Free recall task

This test was presented at the beginning of a test battery. The participants were shown a list of 20 words presented at a rate of one every two seconds. At the end of the list, the subject had two minutes to write down (in any order) as many of the words as possible on the sheet provided. The variables generated in this task included the number of words written down, the number of correct words and recall position.

Variable fore-period simple reaction time task

In this task, a box was displayed in the centre of the screen and at varying intervals (from 1-8 seconds), a target square would appear in the box. As soon as they detected the square, participants were required to press a response key using the forefinger of their dominant hand only. This task lasted for approximately 3 minutes. A measure of mean reaction time was recorded for each minute of performance. A total mean reaction time was also calculated from the total number of trials completed during the whole test. Responses below 200 ms and greater than 750 ms were eliminated from the calculation of these variables.

Repeated digits vigilance task

This visual cognitive vigilance task measured the ability to detect targets at irregular intervals. In this task, participants were shown successive presentations of three-digit numbers in the centre of the screen (e.g., 473) at the rate of 100 per minute. Each three-digit number usually differed from the one immediately preceding it, with one out of the three digits being replaced with a different digit (e.g., 463, 563, 562). Occasionally (eight times a minute), the same three-digit number was presented on successive trials. Participants were instructed to detect these repetitions and respond as quickly as possible by pressing the space bar on the keyboard using the forefinger of their dominant hand. The task lasted for 3 minutes. The number of targets detected (hits), mean reaction time to target and number of false alarms were recorded for the duration of the task and for each minute of task performance.

Serial reaction time task

This task was a measure of both speed and accuracy of movement to different targets. Five buttons were arranged on the response board in a regular pentagon, with a sixth button in the centre. A light appeared on one of the peripheral buttons. The participant was required to press the illuminated button using the forefinger of their dominant hand only. Following this, the centre key became illuminated. The participant was then required to press this central light and continue to follow the light around the board in this periphery button, central button, and periphery button sequence. This task lasted for 3 minutes. The variable assessed in this task was the percentage of trials correctly performed.

Focused attention

This choice reaction time task measures various aspects of selective attention. In this task, target letters appeared in upper case A's and B's in the centre of the screen. Participants were required to respond to the target letter presented in the centre of the screen, ignoring any distracters presented in the periphery as quickly and as accurately as possible. The correct response to A was to press a key with the forefinger of the left hand, while the correct response to B was to press a different key with the forefinger of the right hand. Prior to each target presentation, three warning crosses were presented on

the screen, and the outside crosses were separated from the middle one by either 1.02 or 2.60 degrees. The crosses were on the screen for 500 ms and were then replaced by the target letter. The central letter was either accompanied by 1) nothing, 2) asterisks, 3) letters which were the same as the target or 4) letters which differed from the target. The two distracters presented were always identical, and the targets and accompanying letters were always A or B.

Participants were given ten practice trials followed by five blocks of 64 trials. In each block, there were equal numbers of near / far conditions, A or B responses and equal numbers of the four distracter conditions. The nature of the previous trial was controlled. This test lasted approximately 8 minutes.

In this task, several aspects of choice responses to a target were measured. The global measures of choice reaction time that were assessed were mean reaction time and accuracy of response (per cent correct) when the target was presented alone or when distracters were present. In addition, a measure of selective attention was recorded, e.g., the Erikson effect. This provides a measure of focusing of attention, describing the effect of spatial interference caused by disagreeing stimuli placed near to or far from the target upon reaction time and accuracy of response to the target. If attention is focused, then a big difference between near and far distractor conditions should be found. If attention is set to a wide angle, then this difference should be reduced. A more specific aspect of choice response was measured, recording choice reaction time and accuracy with which new information was encoded, i.e., the difference in reaction time and accuracy of response between conditions when the target is alternated from the previous trial and when the target is repeated from the previous trial.

Categoric Search

This task was similar to the focused attention task previously outlined. Each trial started with the appearance of two crosses either in the central positions occupied by the non-targets in the focused attention task, i.e., 2.04 or 5.20 degrees apart or further apart, located towards either left or right extremes of the screen. The target letter would then appear in place of one of these crosses. However, in this task, participants did not know where the target would appear. On half the trials, the target letter A or B was presented alone, and on the other half, it was accompanied by a distracter, in this task, a digit (1-7). Again, the number of near/far stimuli, A versus B responses and digit/blank conditions were controlled. Half of the trials led to compatible responses (i.e., the letter A on the left side of the screen or the letter B on the right), whereas the others were incompatible. The nature of the preceding trial was also controlled. In other respects (practice, number of trials, etc.), the task was identical to the focused attention task. This task also lasted approximately 8 minutes.

As in the focused attention task, several aspects of choice response to a target were measured. The global measures were choice reaction time and accuracy of response when the target was presented alone in either near or far locations. A more specific aspect of choice response was measured, recording choice reaction time and accuracy with which new information was encoded. In addition, specific aspects of selective attention were measured. For each of these variables outlined below, mean reaction time and accuracy were calculated. A measure of response organisation was recorded. This refers to the effect of compatibility of the target position and the response key upon reaction time and accuracy. A further measure of place repetition was taken, which refers to the effect of the target location (i.e., the target appearing in the same or a different place on successive trials). A measure of spatial uncertainty was also taken, which describes the extent to which not knowing the location of the target (in near or far locations) hinders both reaction time and accuracy.

Verbal reasoning

Participants were presented with statements about the order of the letters A and B followed by the letters AB or BA (e.g., A follows B: BA). The participants were required to read the statement and decide whether it was a true description of the order of the letters. If it was, the participant was required to press the T key on the keyboard; if it was not, they were required to press the F key. The sentences ranged in syntactic complexity from simple active to passive negative (e.g., A is not followed by B). This task lasted approximately 3 minutes. The global variables derived from this test were the total number of trials done and the percentage of correct responses. Additional variables were mean reaction time and percentage accuracy of trials for sentence complexity and true and false sentences.

Semantic memory

This measured the speed of retrieval of information from general knowledge. Participants were shown a sentence, and they had to decide whether it was true (e.g., canaries have wings) or false (e.g. dogs have wings). This task lasted approximately 3 minutes. The variables measured were the total number of trials completed, the percentage of correct trials and the mean reaction time of correct and wrong responses.

Recognition memory

This test was presented at the end of the test session. Participants were shown 40 words that consisted of the 20 words shown in the free recall task at the start of the test battery, plus 20 distracters. The participants were required to decide as quickly as possible whether each word had been shown in the original list or not by pressing the true or false keys. The variables measured were the number of target words correct and non-target words wrong and the mean reaction time of target and non-target words guessed correctly and wrongly.

Analysis Strategy

Initial analyses examined whether those with an illness differed from the healthy controls in terms of demographics, psychosocial factors, and health-related behaviours. Comparisons were then made for the symptoms and signs of the illness and healthy groups. Performance and mood data were analysed using analyses of covariance. Between-subject analysis was employed to:

a) Compare performance effects between healthy participants and those volunteers suffering from an acute illness.
b) Examine the effects of different acute symptoms on aspects of performance and compare these to the healthy control group

RESULTS

Experimental groupings

Sixty participants completed the study.
For the analyses comparing the acute illness group and the healthy controls, all participants were included, as shown in Figure 1. Then, for the analyses assessing the effect of the individual acute illness on mood and performance compared to healthy controls, 6 participants with a mixture of symptoms were excluded, as the illness could not easily be categorised. The remaining participants were grouped as follows: 6 participants were examined with a sore throat, 3 participants were examined with a cough, 6 participants were examined with a headache, and 39 were tested as healthy controls. These experimental groupings are shown in Figure 2.

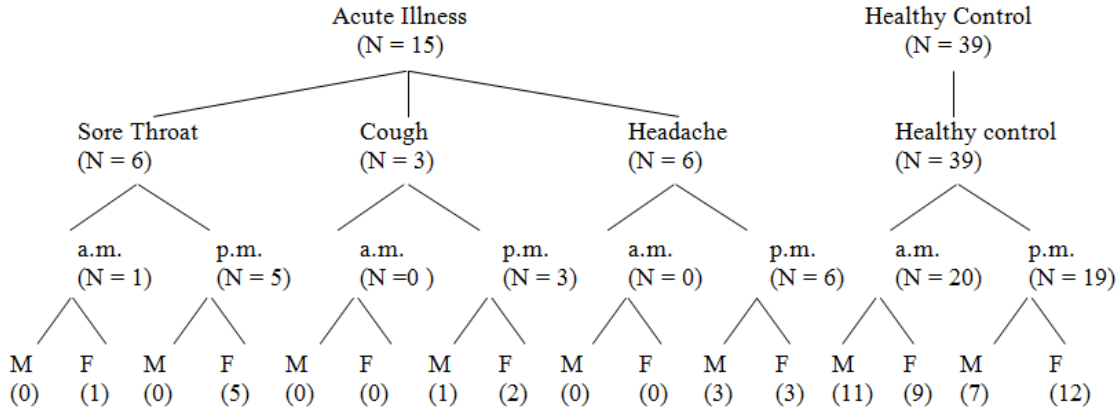

Figure 2: Experimental groupings for analyses comparing individual acute illness groups and healthy controls.

Differences between demographics, personality measures, psychosocial factors and health-related behaviours in those with acute illnesses and healthy controls

Preliminary analyses (t-tests and chi-square) revealed that of the 268 variables assessed, only 5.97% showed significant differences between those who suffered from an acute illness and the healthy controls on measures of demographics, personality and psychosocial factors and health-related behaviours. Given the number of variables analysed, these effects would be expected by chance. Those who were ill reported a greater intensity of hassles, more somatic symptoms, more cognitive failures and were less likely to eat breakfast on a daily basis.

Measures of signs, pain and symptoms

Measures included in these analyses were the individual pain and symptom ratings, a total pain score, a total symptom score, a total score from symptoms indicative of upper respiratory tract infections (URTI) and a total score from the remaining non-URTI symptoms on the checklist. Additional factor scores included fatigue, sub-lingual temperature, nasal, throat, nausea, cough and earache. Headache was also included as a single item.

The URTI symptom measure consisted of the total symptom scores of the following symptoms: pain in the chest, sore throat, headache, sneezing, runny nose, blocked nose, hoarseness, cough, hot/cold, sweating, shivering, fever and phlegm.

The non-URTI measure consisted of the total score of the following symptoms: physical weakness, excessive fatigue, legs feeling heavy, muscle pain in back, arms or legs, painful joints, nausea, indigestion, bloated stomach, wind, diarrhoea, earache, sore eyes, sensitive to noise, sensitive to light, swollen glands, racing heart, insomnia, depression, anxiety/panic feelings, loss of concentration, loss of memory, allergies, dizziness, faintness and loss of appetite.

The fatigue measure consisted of the total score of the following symptoms: physical weakness, hot/cold, shivering, sweating and fatigue.
The nasal measure consisted of the total score of sneeze and blocked nose.

The throat measure consists of the total score of hoarse and sore throat.

The sub-lingual temperature, nausea, cough, earache, and headache measures consisted of the individual item scores.

Differences between pre and post-performance measures of signs, pain and symptoms in those with acute illnesses and healthy controls

At Visit 1 (ill test session), significant differences were found from the t-test analyses between those who suffered from an acute illness and the healthy controls in terms of self-reported measures of pain and symptoms (see Table 2 for pre-performance measures and Table 3 for post-performance measures of the total and individual scores included in the analyses).

Participants in the acute illness group reported a greater overall score on the pain scales, a greater number of total symptoms, URTI symptoms and non-URTI symptoms compared to the healthy control group on both pre and post-performance measures. This pattern was also observed for each of the individual scores examined. No differences were found between pre- and post-performance measures of sub-lingual temperature, suggesting that those in the acute illnesses group were not suffering from influenza.

For Visit 2 (healthy test session), t-test analyses revealed that of the 120 variables assessed, only one showed significant differences between those who suffered from an acute illness and the healthy controls on signs and self-reported measures of pain and symptoms. Given the number of variables analysed, this effect would be expected by chance.

Table 2: Visit 1 (Ill test session): Comparisons of *pre-performance* ratings of pain and symptom severity scores in those with acute illnesses (grouped) and healthy controls.

	Healthy		Ill		t Statistic		
	Mean (s.d.)	N	Mean (s.d.)	N	t	P	df
Total pain score	0.03(0.03)	39	17.71(3.40)	21	-7.15	0.0001	1,58
Total symptom score	2.79(0.83)	39	16.71(3.12)	21	-5.48	0.0001	1,58
Total URTI score	0.59(0.35)	39	6.86(1.25)	21	-6.10	0.0001	1,58
Total non-URTI score	2.21(0.59)	39	9.86(2.34)	21	-4.06	0.0001	1,58
Nausea	0 (0)	39	0.05(0.05)	21	-1.37	NS	1,58
Headache	0.08(0.06)	39	1.33(0.30)	21	-5.36	0.0001	1,58
Earache	0(0)	39	0.48(0.24)	21	-2.78	0.01	1,58
Cough	0.05(0.04)	39	0.95(0.25)	21	-4.72	0.0001	1,58
Fatigue	0.79(0.19)	39	2.57(0.59)	21	-3.52	0.001	1,58
Nasal	0.05(0.04)	39	0.57(0.24)	21	-2.81	0.01	1,58
Throat	0(0)	39	1.71(0.37)	21	-6.32	0.0001	1,58
Sub-lingual temperature (°C)	36.71(0.07)	39	36.83(0.08)	21	-1.10	NS	1,58

Table 3: Visit 1 (Ill test session): Comparisons of *post-performance* ratings of pain and symptoms severity scores in those with acute illnesses (grouped) and healthy controls.

	Healthy		Ill		t Statistic		
	Mean (s.d.)	N	Mean (s.d.)	N	t	P	df
Total pain score	0.15(0.15)	39	13.71(2.92)	21	-6.35	0.0001	1,58
Total symptom score	3.44(0.88)	39	16.57(2.96)	21	-5.33	0.0001	1,58
Total URTI score	0.59(0.29)	39	5.95(0.97)	21	-6.60	0.0001	1,58
Total non-URTI score	2.85(0.73)	39	10.62(2.27)	21	-4.01	0.001	1,58
Nausea	0(0)	39	0(0)	21			
Headache	0.15(0.07)	39	1.38(0.29)	21	-5.33	0.0001	1,58
Earache	0(0)	39	0.62(0.24)	21	-3.49	0.001	1,58
Cough	0.03(0.03)	39	0.62(0.20)	21	-3.94	0.001	1,58
Fatigue	1.00(0.21)	39	2.95(0.52)	21	-4.06	0.0001	1,58
Nasal	0.03(0.03)	39	0.33(0.17)	21	-2.34	0.05	1,58
Throat	0(0)	39	1.81(0.36)	21	-6.98	0.0001	1,58
Sub-lingual temperature (°C)	36.61 (0.07)	39	36.64(0.09)	21	-0.26	NS	1,58

Differences between pre and post-performance measures of signs, pain and symptoms in those with specific acute illnesses (sore throat, cough and headache) and healthy controls

At Visit 1 (ill test session), significant differences were found from the analysis of variance between those who suffered from sore throats, coughs and headaches and the healthy controls in terms of self-reported measures of pain and symptoms (see Table 4 for pre-performance measures and Table 5 for post-performance measures of the total and individual scores included in the analyses).

A. Illness groups and healthy controls

Participants in each of the acute illness groups reported a greater overall score on the pain scales, a greater number of total symptoms, URTI symptoms and non-URTI symptoms compared to the healthy control group on both pre and post-performance measures. This pattern was

also observed for each of the factor scores examined. No differences were found between pre and post-performance measures of sub-lingual temperature, suggesting that those in the acute illnesses group were not suffering from influenza.

B. Differences between individual acute illnesses on measures of pain and symptom severity

Several differences were identified between those participants reporting a headache, cough and sore throat on measures of pain and symptom severity. These findings (outlined below) suggest that each of the three acute illnesses assessed was associated with specific illness characteristics.

i) Symptom severity scores

- Participants in the sore throat group rated greater symptom scores on measures of earache, non-URTI symptoms and throat than both headache and cough conditions.
- Participants in the cough group rated greater symptom scores on measures of cough, nasal and URTI symptoms than both headache and sore throat conditions.
- Participants in the headache group rated greater symptom scores on measures of headache and fatigue than both sore throat and cough conditions.

ii) Ratings of pain

The greatest ratings of pain were reported in the sore throat and headache conditions compared to participants in the cough and healthy control groups. Further distinctions were made between the three acute illness groups in terms of the individual items on the pain scale, as outlined below.

- Participants in the sore throat group rated greater symptom scores on measures of dull pain, tender, raw, sore, aching and irritated than both headache and cough conditions.
- Participants in the cough group rated greater symptom scores on a measure of burning than both headache and sore throat conditions.
- Participants in the headache group rated greater pain scores on measures of throbbing, thumping, pounding and stabbing than both sore throat and cough conditions.

For Visit 2 (healthy test session), no significant differences were found from the analysis of variance between those who suffered from specific acute illnesses (sore throat, cough and headache) and the healthy controls on both pre-and post-performance measures of signs and self-reported measures of pain and symptoms.

Table 4: Visit 1 (Ill test session): Comparisons of *pre-performance* ratings of pain, symptom severity and signs in those with acute illnesses of sore throat, cough and headache and healthy controls.

	Healthy control		Sore throat		Cough		Headache		
	Mean (s.e.)	**N**	**Mean (s.e.)**	**N**	**Mean (s.e.)**	**N**	**Mean (s.e.)**	**N**	**ANOVA**
Total pain score	0.03 (0.03)	39	25.67 (8.77)	6	9.33 (3.67)	3	17.83 (6.96)	6	F (3,50) = 19.81, p<0.0001
Total symptom score	2.80 (0.83)	39	17.17 (6.66)	6	18.00 (8.39)	3	18.83 (7.94)	6	F (3,50) = 9.00, p<0.0001
Total URTI score	0.59 (0.35)	39	6.00 (2.10)	6	10.67 (4.91)	3	7.67 (2.91)	6	F (3,50) = 13.57, p<0.0001
Total non-URTI score	2.21 (0.59)	39	11.17 (6.19)	6	7.33 (3.48)	3	11.17 (5.16)	6	F (3,50) = 5.02, p<0.01
Nausea	0 (0)	39	0 (0)	6	0 (0)	3	0.17 (0.17)	6	
Headache	0.08 (0.06)	39	0.83 (0.48)	6	1.33 (0.88)	3	2.67 (0.33)	6	F (3,50) = 32.21, p<0.0001
Earache	0 (0)	39	1.33 (0.67)	6	0 (0)	3	0 (0)	6	
Cough	0.05 (0.04)	39	0.67 (0.49)	6	2.00 (0.58)	3	0.67 (0.42)	6	F (3,50) = 12.77, p<0.0001
Fatigue	0.80 (0.19)	39	1.50 (0.76)	6	3.33 (1.67)	3	3.67 (1.65)	6	F (3,50) = 5.51, p<0.01
Nasal	0.05 (0.04)	39	0.50 (0.50)	6	1.00 (1.00)	3	0.67 (0.49)	6	F (3,50) = 3.37, p<0.05
Throat	0 (0)	39	2.67 (0.88)	6	2.33 (0.67)	3	0.17 (0.17)	6	F (3,50) = 30.12, p<0.0001
Sub-lingual temperature (°C)	36.71 (0.07)	39	36.62 (0.13)	6	36.90 (0.45)	3	36.90 (0.09)	6	NS

Table 5: Visit 1 (Ill test session): Comparisons of *post-performance* ratings of pain, symptom severity and signs in those with acute illnesses of sore throat, cough and headache and healthy controls.

	Healthy control		Sore throat		Cough		Headache		
	Mean (s.e.)	N	Mean (s.e.)	N	Mean (s.e.)	N	Mean (s.e.)	N	ANOVA
Total pain score	0.15 (0.15)	39	22.83 (7.60)	6	6.00 (2.00)	3	11.17 (5.42)	6	F (3,50) = 18.83, p<0.0001
Total symptom score	3.44 (0.88)	39	18.17 (6.71)	6	15.00 (6.00)	3	17.17 (6.74)	6	F (3,50) = 8.40, p<0.0001
Total URTI score	0.59 (0.29)	39	5.67 (1.59)	6	7.67 (2.40)	3	6.17 (2.63)	6	F (3,50) = 13.46, p<0.0001
Total non-URTI score	2.85 (0.73)	39	12.5 (6.03)	6	7.33 (3.71)	3	11.0 (4.31)	6	F (3,50) = 4.94, p<0.01
Nausea	0(0)	39	0(0)	6	0(0)	3	0(0)	6	
Headache	0.15 (0.07)	39	0.83 (0.48)	6	1.33 (0.67)	3	2.17 (0.54)	6	F (3,50) = 15.79, p<0.0001
Earache	0 (0)	39	1.00 (0.63)	6	0 (0)	3	0.67 (0.49)	6	F (3,50) = 5.87, p<0.01
Cough	0.03 (0.03)	39	0.67 (0.33)	6	1.33 (0.88)	3	0.17 (0.17)	6	F (3,50) = 10.77, p<0.0001
Fatigue	1.00 (0.21)	39	2.67 (0.80)	6	2.33 (1.45)	3	3.67 (1.52)	6	F (3,50) = 4.72, p<0.01
Nasal	0.03 (0.03)	39	0.17 (0.17)	6	0.67 (0.67)	3	0.50 (0.50)	6	F (3,50) = 2.95, p<0.05
Throat	0 (0)	39	3.00 (0.68)	6	1.67 (0.67)	3	0.33 (0.21)	6	F (3,50) = 47.62, p<0.0001
Sub-lingual temperature (°C)	36.61 (0.07)	39	36.40 (0.13)	6	36.87 (0.47)	3	36.73 (0.12)	6	NS

Differences between acute illnesses (sore throat, cough and headache) and healthy controls on measures of sleeping and eating prior to each test session

No differences were found between the acute illness and healthy control groups in terms of sleeping or eating practices prior to each of the test sessions.

Differences between the healthy and acute illness groups on measures of mood and performance

Those who were ill reported lower levels of alertness and reduced hedonic tone both before and after the performance tests. They had slower response times in the simple reaction time, focused attention and categoric search tests. In addition, they had a higher error rate on the verbal reasoning task and missed more targets in the repeated digits detection task. Free recall, delayed recognition memory, semantic memory and performance of a serial response task were unimpaired (see Table 6).

Table 6: Effects of illness on mood and performance (Scores are the adjusted means from the covariance analyses, s.e. shown in parentheses).

(a) Significant effects

MEASURE		ILL	HEALTHY	ANCOVA
		(N = 21)	(N = 39)	
(1)	Pre-performance mood			
	(a) Alertness	185.9 (8.8)	261.1 (6.4)	F (1,57) = 47.6, p<0.0001
	(b) Hedonic tone	169.9 (6.2)	203.2 (4.5)	F (1,57) = 18.9, p<0.0001
(2)	Post-performance mood			
	(a) Alertness	165.3 (8.5)	217.4 (6.2)	F (1,57) = 24.2, p<0.0001
	(b) Hedonic tone	167.8 (6.6)	183.1 (4.8)	F (1,57) = 3.5, p<0.05

(3)	Simple reaction time (ms)	323 (7.7)	305 (5.6)	F (1,57) = 3.5, p<0.05
(4)	Focused attention			
	(a) Mean reaction time taken to identify targets presented alone or with an asterisk (ms)	387 (4.5)	372 (3.2)	F (1,57) = 6.97, p<0.05
	(b) Mean reaction time taken to identify targets with distractors present (ms)	395 (5.0)	383 (3.6)	F (1,57) = 3.7, p<0.05
	(c) Mean reaction time taken to identify targets presented alone (ms)	388 (5.1)	372 (3.7)	F (1,77) = 6.86, p<0.05
(5)	Categoric search			
	(a) Compatibility effect (ms)	23 (3.4)	33 (2.5)	F (1,57) = 5.95, p<0.05
	(b) Reaction time to identify targets in blank and compatible conditions (ms)	427 (6.9)	411 (5.0)	F (1,57) = 3.5, p<0.05
(6)	Verbal reasoning – percentage of trials correct	80.4 (1.7)	85.2 (1.2)	F (1,57) = 5.12, p<0.05
(7)	Repeated digits detection task - number of targets hit (maximum = 24)	13.9 (0.7)	15.7 (0.5)	F (1,57) = 4.43, p<0.05

(b) Non-significant results

	MEASURE	**ILL (N = 21)**	**HEALTHY (N = 39)**	**ANCOVA**
(1)	Pre-performance mood – anxiety	88.8 (3.5)	92.4 (2.6)	NS
(2)	Post-performance mood – anxiety	87.0 (3.8)	89.5 (2.8)	NS
(3)	Serial reaction time			
	(a) Total number of responses	384 (7.0)	397 (5.1)	NS
	(b) Percentage of trials correct	99.3 (0.2)	99.4 (0.1)	NS
	(c) Number of long responses	0.03(0.02)	0.00 (0.01)	NS
(4)	Focused attention			
	(a) Mean reaction time taken to encode new information (ms)	18.8 (3.6)	15.3 (2.6)	NS
	(b) Mean reaction time taken to focus attention (ms) (Erikson effect)	7.1 (6.4)	12.3 (4.7)	NS
	(c) Mean accuracy to targets presented alone or with an asterisk (max = 5)	4.66(0.03)	4.73 (0.02)	NS
	(d) Mean accuracy to targets with distractors present (max = 5)	4.54(0.05)	4.63 (0.03)	NS
	(e) Number of long responses (> 800 ms)	4.75 (0.8)	3.5 (0.6)	NS
	(f) Number of errors	14.8 (2.3)	14.1 (1.7)	NS
(5)	Categoric search			
	(a) Mean reaction time to targets presented alone or with an asterisk (ms)	500 (6.2)	491 (4.5)	NS
	(b) Mean reaction time taken to encode new information (ms)	19.9 (3.9)	16.1 (2.8)	NS
	(c) The effect of spatial uncertainty on reaction time (ms)	74.7 (6.6)	87.6 (4.9)	NS
	(d) The effect of place repetition on reaction time (ms)	18.7 (4.9)	9.9 (3.6)	NS
	(e) Mean accuracy to targets presented alone or with an asterisk	4.59(0.04)	4.60 (0.03)	NS
	(f) Number of long responses (> 800 ms)	4.25 (1.0)	5.22 (0.7)	NS
	(g) Number of errors	21.5 (2.2)	20.4 (1.6)	NS
(6)	Verbal reasoning speed (number done)	55.3 (1.9)	54.7 (1.4)	NS
(7)	Semantic processing speed (number done)	111.2(2.3)	111.4 (1.7)	NS

(8)	Free recall – number of trials correct (maximum = 20)	7.2 (0.4)	8.0 (0.3)	NS
(9)	Recognition memory			
	(a) Number of hits (max = 20)	14.6 (0.5)	15.8 (0.4)	NS
	(b) Number of false alarms	5.6 (0.5)	5.6 (0.4)	NS
	(c) Mean reaction time of target words hits (ms)	852 (27)	789 (20)	NS
	(d) Mean reaction time of target words missed (ms)	921 (51)	942 (38)	NS
	(e) Mean reaction time of correct rejections (ms)	837 (30)	897 (22)	NS
	(f) Mean reaction time of false alarms (ms)	904 (47)	894 (32)	NS
(10)	Repeated digits			
	(a) Number of false alarms	3.5 (0.6)	3.9 (0.4)	NS
	(b) Mean reaction time of targets hit (ms)	558 (11.2)	569 (8.2)	NS

Differences between the healthy and different acute illnesses (sore throat, cough and headache) on measures of mood and performance

Analyses of the effects of the individual illnesses showed that there were some global effects that were apparent in all illnesses (e.g., more negative mood, and slower reaction time in the focused attention task). Headache was associated with the greatest impairments. Specifically, in the headache group, free recall was impaired and sustained attention worse (slower performance on the serial response task, more misses on the repeated digits task, and more momentary lapses of attention on the focused attention task). Those with a sore throat were less accurate on the logical reasoning task. These results are shown in Table 7.

Table 7: Effects of different illnesses on mood and performance (Scores are the adjusted means from the covariance analyses, s.e. shown as bars)

A. Mood: All illnesses were significantly different from healthy

Measure	Sore-throat (N = 6)	Headache (N = 6)	Cough (N = 3)	Healthy (N = 39)
Pre-performance mood - alertness	184.6 (17.2)	163.9 (17.3)	214.0 (24.2)	261.4 (6.7)
Pre-performance mood - hedonic tone	172.0 (12.1)	157.6 (11.9)	165.7 (16.7)	203.6 (4.6)
Post-performance mood - alertness	173.6 (17.2)	158.4 (16.6)	171.1 (23.7)	218.4 (6.5)

B. Focused attention: All illnesses were significantly different from healthy

Measure	Sore-throat (N = 6)	Headache (N = 6)	Cough (N = 3)	Healthy (N = 39)
Mean reaction time to targets presented alone or with an asterisk (ms)	393.5 (8.3)	391.3 (8.6)	394.3 (11.9)	372.6 (3.2)

C. Tests where only headache was significantly worse than all other conditions

	Sore-throat (N = 6)	Headache (N = 6)	Cough (N = 3)	Healthy (N = 39)
Free recall - number of words correct (max = 20)	8.3 (0.8)	6.4 (0.8)	8.0 (1.1)	8.0 (0.3)
Serial reaction time - number of trials completed	402.2 (13.0)	367.6 (13.0)	397.3 (18.4)	398.4 (5.1)
Repeated digits detection – number of targets hit (max = 24)	15.4 (1.3)	12.2 (1.3)	14.9 (1.9)	15.7 (0.5)
Focused attention – number of long responses (> 800 ms)	3.0 (1.3)	8.9 (1.4)	2.5 (1.8)	3.5 (0.5)
Focused attention – number of errors	13.9 (4.4)	23.1 (4.4)	7.1 (6.2)	14.2 (1.7)

D. Tests where sore throat was significantly worse than healthy controls

	Sore-throat (N = 6)	Headache (N = 6)	Cough (N = 3)	Healthy (N = 39)
Verbal reasoning – percentage of trials correct	74.2 (3.1)	81.3 (3.2)	82.5 (4.4)	84.9 (1.2)

DISCUSSION

Previous research with both experimentally induced MURTIs and naturally occurring illnesses has demonstrated reduced alertness and impaired cognitive performance. This finding was confirmed in the present study, and additional results suggested more global impairments than had been observed in the earlier studies. Tasks involving the speed of response are usually most impaired when the person has a MURTI. Sustained attention and verbal reasoning were also impaired in the present study. Analysis of specific symptoms showed very few effects related only to those

symptoms. The exception was headache, where memory and attention were also impaired. This effect of headache confirms results from a previous study.[52]

The study has several limitations. First, the sample size was small, and the absence of effects of specific symptoms may reflect the small numbers in those groups. Secondly, there was only one time point during the illness, and it would have been better to examine the effects during the illness. The study did not attempt to identify underlying mechanisms, although this has been done in the earlier research. It will be interesting to determine whether OTC treatment of MURTIS, for example, using compounds with aromatic vapours, removes the behavioural malaise associated with the illness. The mood changes induced by the illness, especially the reduced alertness, were observed with all symptoms and are a good starting point for therapeutic efficacy studies. The present methodology can also be applied to other infections of current concern, such as COVID.[53]

CONCLUSION

Mild upper respiratory tract illnesses (MURTIs) lead to malaise, which reflects reduced well-being, fatigue, and impaired performance. This was investigated in the present study. The MURTI group were less alert, had a more negative mood, and had slower reaction times. They also detected fewer targets in a sustained attention task and had a lower percentage correct on a verbal reasoning task. Specific comparisons were then made between the different symptom groups (sore throat, cough and headache). All symptom groups reported lower alertness than the healthy group. The headache group had the greatest impairments, with poorer free recall and problems of attention. Future research must now determine whether therapies can remove the malaise associated with MURTIs.

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