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The influence of shift work on cognitive functions and oxidative stress

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ABSTRACT

Shift work influences health, performance, activity, and social relationships, and it causes impairment in cognitive functions. In this study, we investigated the effects of shift work on participants' cognitive functions in terms of memory, attention, and learning, and we measured the effects on oxidative stress. Additionally, we investigated whether there were significant relationships between cognitive functions and whole blood oxidant/antioxidant status of participants. A total of 90 health care workers participated in the study, of whom 45 subjects were night-shift workers. Neuropsychological tests were administered to the participants to assess cognitive function, and blood samples were taken to detect total antioxidant capacity and total oxidant status at 08:00. Differences in anxiety, depression, and chronotype characteristics between shift work groups were not significant. Shift workers achieved significantly lower scores on verbal memory, attention–concentration, and the digit span forward sub-scales of the Wechsler Memory Scale-Revised (WMS-R), as well as on the immediate memory and total learning sub-scales of the Auditory Verbal Learning Test (AVLT). Oxidative stress parameters were significantly associated with some types of cognitive function, including attention–concentration, recognition, and long-term memory. These findings suggest that night shift work may result in significantly poorer cognitive performance, particularly working memory.

1. Introduction

Shift work is an employment schedule designed to maintain service or production through 24 h in the day during the whole week (Pati et al., 2002). Employees assigned into shift groups can alternate across early morning, afternoon or night shifts. Over the last several decades, various conditions in work life such as technological improvement, competitive environments, and social conditions of workers, as well as necessity for service continuation, resulted in a rapid increase in the number of shift workers in labor markets all over the world (Almondes and Araujo, 2009). Hospitals are among the institutions in which the work shift schedules have been widely adopted in order to maintain service day and night (Josten et al., 2003).

Shift work has been associated with a number of health problems that have biological, psychological, and sociological aspects. Researchers have shown that shift work leads to negative physiological and psychological outcomes caused by disturbances in the biological rhythm. These problems can be listed as immune system disorders, metabolic disturbances, gastrointestinal symptoms, and cardiovascular diseases (Knutsson, 2003; Blachowicz and Letizia, 2006). Shift work also seems to be a potential risk factor for increased psychiatric morbidity such as somatization, anxiety, interpersonal sensitivity, and low quality of life among health workers (Selvi et al., 2010).

There is evidence in the literature of the physiological and psychological effects of shift work, including sleep disorders, health problems, disruption to biological rhythm, reduced work efficiency, job dissatisfaction, and social isolation. These effects in a hospital setting can easily be predicted to lead to decreased quality of care and ultimately to higher health care costs (AbuAlRub, 2004; Berger and Hobbs, 2006).

Although night-shift work is not rare among healthcare workers, night work is associated with difficulties in performing routine tasks, poor performance, and increased accidents and injuries (Admi et al., 2008). Shift work among hospital nurses is particularly related to shift-work disruption because the shifts change from on to off frequently, and most night shift nurses return immediately to day-activity. Shift working nurses in four hospitals reported being excessively sleepy (Suzuki et al., 2005). In addition,

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night-shift work accompanied by extended working time was found to be associated with an increased risk of patient mortality in hospitals (Trinkoff et al., 2011).

There are significant associations between neurocognitive deficits and night shift work due to greater losses in total sleep time, sleepiness, and fatigue after working all night (Akerstedt and Wright, 2009; Selvi et al., 2010). Possible mechanisms playing a role in the adverse effects of shift work on cognitive functions have been increasingly recognized. Research has consistently evidenced that sleep deprivation resulting from night shift work seems to be central to the adverse effects in executive functions, attention processes, and working memory (Harrison and Horne, 2000a, 2000b; Kim et al., 2001; Drummond et al., 2001). It has been also demonstrated that sleep-deprived subjects are more prone to underestimate their level of cognitive impairment, whereas individuals in general may overestimate the consequences of deprivation while being only minimally impaired on attention tasks (Dinges et al., 1997; Leproult et al., 2003).

Oxidative stress (OS) refers to an imbalance between the systemic secretion of reactive oxygen species and a biological system's ability to detoxify itself or to repair the resulting cell damage through the production of peroxides and free radicals (Punchard and Kelly, 1996). In humans, the brain and neurons are particularly vulnerable to radical-mediated damage (Cui et al., 2004). Reactive oxygen species (ROS) are produced in metabolic and physiological processes, and harmful oxidative reactions may occur in organisms that cannot remove ROS via enzymatic and nonenzymatic antioxidative mechanisms. If the production of free ROS exceeds the system's total antioxidant capacity, then OS occurs (Roenneberg, 2003). OS is known leading to several acute and chronic disorders. It has been well-documented that free oxygen radicals increase in psychiatric disorders such as panic disorder, schizophrenia, and depression, whereas antioxidants such as superoxide dismutase, catalase, glutathione peroxidase, and glutathione reductase decrease concomitantly (Ng et al., 2008; Wood et al., 2009).

Sleep is central to renovation of the antioxidant defense system. OS resulting from a lack of sleep plays a pivotal role in the development of immune system disorders that have higher prevalence in shift workers (Sharifian et al., 2005). The relationship between insomnia and OS seems to be bidirectional: OS might cause insomnia, and, in turn, insomnia might further accelerate OS (Gulec et al., 2012). This study was designed to investigate the effects of working night shifts on total antioxidant (TAC) and oxidant capacity and to evaluate the correlations between neuropsychological test performance following shifts and the examined variables for each type of working schedule.

2. Methods

2.1. Participants and study design

Participants were 90 health care workers, of whom 45 were daytime workers, working at Yüzüncü Yıl University Education and Research Hospital. Inclusion criteria for the study were as follows: not being pregnant, not being under 18 or above 65 years old, not having a history of substance abuse or dependence, no use of medicine for any psychiatric disorders, and having been working in the facility for at least one year.

Daytime workers were recruited from the volunteer health workers and nurses who worked during the daytime, and shift workers were selected from health workers and nurses who consistently rotated between 08:00–16:00 and 16:00–08:00 shifts for 3-week intervals. Individuals who worked during the day shifts or the night shifts were determined by hospital management. Shift workers were selected from employees who volunteered and whose conditions were appropriate for working rotating shifts. Participants in the night shift group were at work during 08:00–16:00 for 3 weeks and then switched to 16:00–08:00 shifts for 3 weeks. Individuals in the night shift group worked 3 days a week and participants in the daytime group worked 5 days a week. All subjects in the shift work group had been on the night schedule for 2 weeks at the time of assessment.

Neuropsychological tests were administered to participants by a clinical psychologist at 08:00. This time was deliberately selected for assessing cognitive performance to assess the possible influence of sleep deprivation caused by night shift work as compared to daytime workers, who were assumed to have an ordinary sleep pattern. We primarily investigated differences in cognitive performance and oxidative stress, and the relations between these variables in the group of night-shift workers after the shift probably emerged because of sleep deprivation. Shift workers completed the neuropsychological tests after the night shift, and daytime workers were administered the tests at the start of their work day. The Wechsler Memory Scale, Auditory-Verbal Learning Test, and Stroop Test were administered to the participants to assess cognitive functioning. Each testing session took an average of 45 min. After the assessment, blood samples were obtained with a hemogram tube to identify total antioxidant capacity (TAC) and total oxidant status (TOS). To evaluate the TAC and TOS, the blood samples were stored at $-80\ ^{\circ}C$ in the freezer.

The study protocol received approval from the Ethics Committee of the Faculty of Medicine, Yüzüncü Yıl University. All participants gave written informed consent after receiving a complete description of the study protocol. The subjects were not paid for their participation.

2.2. Blood sampling and testing

Blood samples were collected in order to determine TAC, TOS, and OSI. Between 08:00 and 09:00, 2-ml samples of venous blood were taken from each participant and placed into tubes with ethylenediaminetetraacetic acid. The samples were kept in a cool box, at $+4\ ^{\circ}C$, until they were transferred to the laboratory of the Medical Biology Department. The biochemical analyses were performed under the same conditions after preparation of all blood samples. Whole blood samples obtained from each subject were hemolyzed with deionized water. After centrifugation ($4000 \times g$ for 10 min at $+4\ ^{\circ}C$), the pellet was discarded to eliminate cellular debris and the upper supernatant fluid was separated. The supernatant hemolysate was decanted into a clean tube. OS biomarkers (TAC and TOS) in the clear supernatant used for the analysis were measured at this stage. All processes were carried out at $+4\ ^{\circ}C$.

TOS levels were determined spectrophotometrically (Genesys 10 UV Scanning UV/vis Spectrophotometer) at 530 nm using kits (Erel, 2005). In this new colorimetric method, oxidants presented in the sample oxidize the ferrous ion-o-dianisidine complex, yielding ferric ion. The oxidation reaction is enhanced by the presence of excess glycerol in the reaction medium. The ferric ion and xylenol orange generate a colored complex. The results are given as micromolar hydrogen peroxide equivalents per liter ($\mu mol\ H_2O_2$ Equiv./L).

TAC levels were measured spectrophotometrically (Genesys 10 UV Scanning UV/vis Spectrophotometer) at 660 nm using kits (Erel, 2004). This method is based on the bleaching of the distinct color of the 2,2′-azino-bis [3-ethylbenzothiazoline-6-sulfonic acid] (ABTS) radical cation via the action of antioxidants. The precision of this assay is accurate (lower than 3% error rate). The results are expressed as mmol Trolox Equiv./L.

The OSI was used to detect OS. OSI is defined as the ratio of the TOS level to TAC level (Aycicek et al., 2005). Specifically, OSI (arbitrary unit)=TOS ($\mu mol\ H_2O_2$ Equiv./L)/TAC (mmol Trolox Equiv./L). The unit is arbitrary unit (AU).

2.3. Assessment instruments

A sociodemographic questionnaire was developed for this study to assess age, gender, marital status, level of education, years of work, shift-work type, medical history, and family history of psychiatric illness.

The Beck Depression Inventory (BDI) is a self-report inventory that measures the severity of the somatic, emotional, cognitive, and motivational symptoms in depression (Beck et al., 1979). The BDI, which includes 21 items, is scored between 0 and 3 for each item. The maximum BDI score is 63 and the minimum score is 0. Total scores of 17 and above indicate possible depression. The BDI was adapted to Turkish by Hisli (1989).

The Beck Anxiety Inventory (BAI) is a self-report inventory that measures the frequency of physiological and other symptoms of anxiety experienced during the previous week (Beck et al., 1988). The BAI has 21 items scored between 0 and 3. The items are summed to obtain a total score that can range from 0 to 63 in order to classify anxiety as mild, moderate, or severe. The BAI was translated into Turkish by Ulusoy et al. (1998).

The Morningness-Eveningness Questionnaire (MEQ) consists of 19 items pertaining to habitual rising and bed times, preferred times of physical and mental performance, and subjective alertness after rising and before going to bed (Horne and Östberg, 1976). MEQ yields scores ranging from 16 to 86. The Turkish version of the MEQ revealed good psychometric properties (Agargun et al., 2007).

2.3.1. Neuropsychological tests

All subjects were neuropsychologically assessed in a standard procedure by the same clinical psychologist. The clinical psychologist performed a battery of three different neuropsychological tests to all subjects with routinized procedures. These tests are identified below respectively.