Physiological Workload Response of Laboratory Staff during simulated Life Science Processes

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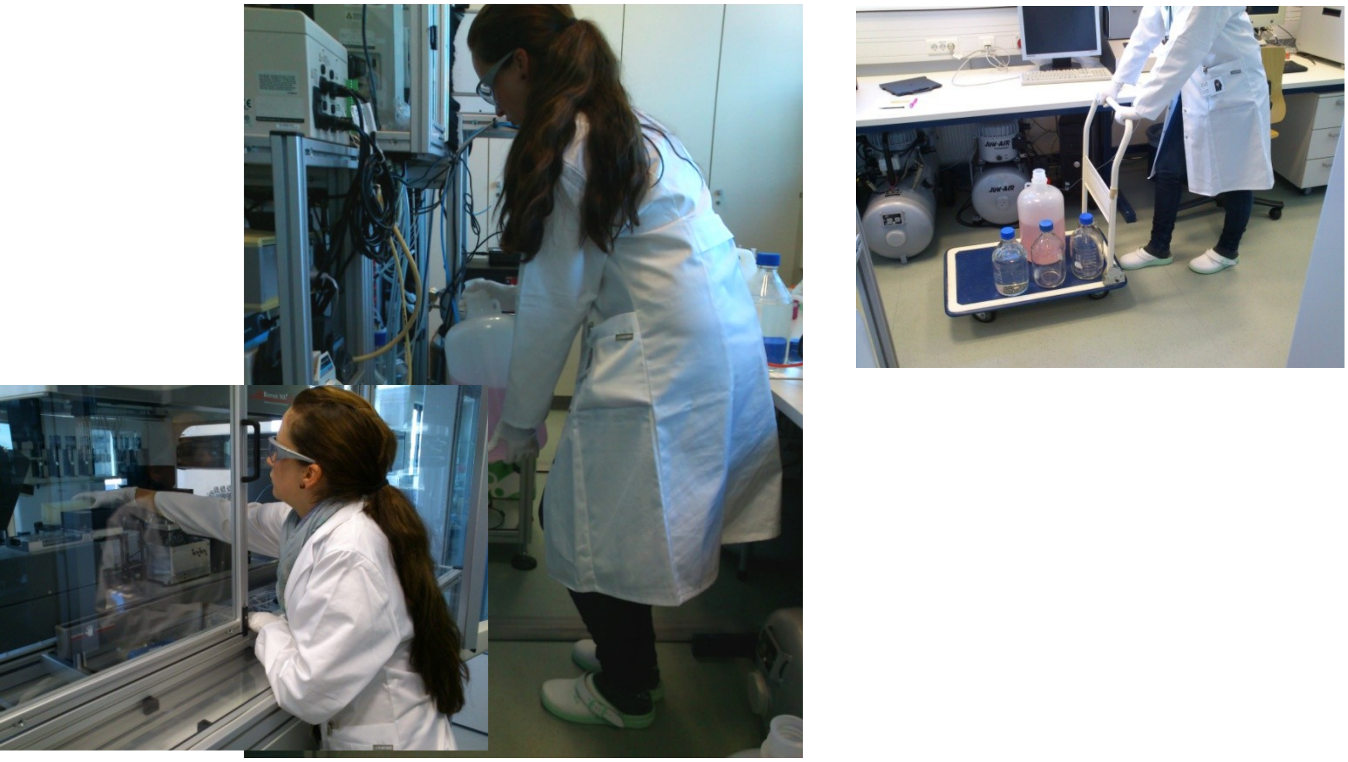
ABSTRACT

High demands for new drug development and advances in robotic technologies have led to automation of compound screening and biological culturing processes in life sciences. Nevertheless, not only cognitive skills during planning, programming, supervision, and evaluation are mandatory but also human manual skills are still essential for system performance in highly automated life science laboratories. Aim of this study was to assess the physiological workload response during simulated cell culturing tasks.
20 healthy volunteers underwent a standardized test protocol including typical cell laboratory tasks. Cardio-respiratory parameters including heart rate (HR), breathing frequency, minute ventilation, oxygen uptake (VO_2) and blood pressure (DBP, SBP) were measured and analyzed.
There were strong effects of task condition on blood pressure (SBP: $F(10,210)=30.8$, $p<0.001$, $\eta^2 = .618$; DBP: $F(10,210)=17.9$, $p=.000$, $\eta^2= .485$), HR ($F(10,210)=34.5$, $p<0.001$; $\eta^2= .793$) and VO_2 ($F(10,210)=253.5$, $p<0.001$; $\eta^2= .969$). Especially during material transportation including static work components, SBP and DBP increased significantly, while HR and VO_2 were significantly elevated during dynamic transportation tasks.
We found significant increases of physiological activation during typical tasks in a modern life science laboratory. During transportation tasks including stepping stairs, average HR reached cut-offs for sustained effort (120 bpm), during all other tasks HR was well below these cut-offs. Episodes of static muscular work during charging and transportation where associated with blood pressure elevations. However, as these muscular loads occur only intermittent during a work shift these elevations seem to be uncritical. Nevertheless, individual assessment is advised for persons at risk.

Keywords: Life Science Automation, Physiological Workload Response, Heart Rate, Blood Pressure, Laboratory Staff, Automated Cell Culturing

INTRODUCTION

High demands for new drug development and advances in robotic technologies have led to automation of compound screening and biological culturing processes in life sciences. Nevertheless, not only cognitive skills during planning, programming, supervision, and evaluation are mandatory but also human manual skills are still essential for system performance in highly automated life science laboratories. Especially before implementing automation to achieve high throughput and high quality standards, prototype processes are usually done manually by human staff. Further, a shift from manual to semi-automated production is not necessarily associated with a reduction in physical loads of the operator. The implementation of biotechnology on an industrial scale can increase physical demands as well because of larger volumes and weights that have to be moved by operators (Fig. 1a-c).



Figures 1a-c: Operator during material handling for a semi-automated cell culturing process

Thus, sensory-motor and muscular demands are still common even in highly automated life science environments. Aim of this experimental study was to assess the physiological workload response during simulated cell culturing tasks.

METHODS

Before starting the experiment several observations during daily routine of a newly implemented semi-automated cell-culturing process were carried out. Table 1 shows the results of the observation study including about 50 work steps.

Table 1. Task analysis of a semi-automated cell-culturing process

Step	Task	Operator
1	Sample preparation	Analyst
1.1	Warming solutions	Analyst
1.1.1	Get solutions from cooling box	Analyst
1.1.2	Put solutions into Cytomat	Analyst
1.2	Prepare BIOMEK Cell-Workstation	Analyst
1.2.1	Human Computer Interaction (HCI)	Analyst
1.2.2	Changing bottles	Analyst
1.2.3	Delete membranes	Analyst

1.2.4	Cover Autoflasks with new membranes	Analyst
1.3	Check cells	Analyst
1.3.1	Change clothes (clean room suite)	Analyst
1.3.2	Put on gloves	Analyst
1.3.3	Desinfect hands	Analyst
1.3.4	Put on safety glassess	Analyst
1.3.5	Get T75 flask from Cytomat/clean room	Analyst
1.3.6	Put off safety glasses	Analyst
1.3.7	Put off glove	Analyst
1.3.8	Change clothes	Analyst
1.3.9	Tranport sample to Lab II	Analyst
1.3.10	Microscoping	Analyst
1.3.10.1	Sample preparation for microscoping	Analyst
1.3.10.2	Put off safety glasses	Analyst
1.3.10.3	Evaluation	Analyst
1.3.10.4	Documentation	Analyst
1.3.10.5	Put on safety glasses	Analyst
1.3.10.6	Put sample beside work bench	Analyst
1.4	Desinfect and charge liquid handler deck	Analyst
2	Cell harvesting	
2.1	Remove used media	BIOMEK Cell Workstation
2.2	Washing with PBS	BIOMEK Cell Workstation
2.3	Incubate sample	BIOMEK Cell Workstation
2.4	Add DMEM and resuspense	BIOMEK Cell Workstation
2.5	Transfer cell suspension into modular reservoir	BIOMEK Cell Workstation
3	Alginate bead production	
3.1	Prepare liquid handler deck/ unpack material	Analyst
3.2	Count cells	BIOMEK Cell Workstation
3.3	Aliqoting of cell suspension	BIOMEK Cell Workstation
3.4	Create counter weight	BIOMEK Cell Workstation
3.5	Centrifugation	BIOMEK Cell Workstation
3.6	Aliqote CaCl2-solution into well plate	BIOMEK Cell Workstation
3.7	Remove supernatant	BIOMEK Cell Workstation
3.8	Transfer alginate into deep-well plate	BIOMEK Cell Workstation
3.9	Resuspense	BIOMEK Cell Workstation
3.10	Remove air bubbles from alginate suspension	BIOMEK Cell Workstation
3.11	Dropping suspension into 96-well plate	BIOMEK Cell Workstation
3.12	Incubation	BIOMEK Cell Workstation
3.13	Remove CaCl2-supernatant	BIOMEK Cell Workstation
3.14	Cover 96-well plate with membrane	Analyst
3.15	Washing	BIOMEK Cell Workstation
3.16	Add DMEM	BIOMEK Cell Workstation
3.17	Transfer samples to Cytomat and choose hotel	Analyst
4	Check alginate bead quality	
4.1	Transfer sample to microscope	Analyst

4.2	Microscope samples and evaluate bead quality	Analyst
5	Transfer samples to Cytomat and choose hotel	Analyst
6	Clean liquid handler	Analyst
7	Document Process and Results	Analyst

20 healthy volunteers (10 female / 10 male) gave their written informed consent to participate. Anthropometric, activity and fitness data of the participants are shown in Table 2. After information and instruction volunteers underwent a standardized test protocol at the Center for Life Science Automation. Baseline measurements during supine, sitting rest were followed by a quasi-natural setup of 9 different tasks typical for life science workplaces, e. g. pipetting, tipping, monitoring processes / computer work (human-computer interaction, HCI), and sample transportation, material handling and cleaning. Tasks were carried out for 5 minutes each. During the experiment participants wore different mobile physiological measuring systems to analyze respiratory gas volumes and ventilation, cardiac activity and blood pressure. Respiratory measurements were carried out using the validated mobile metabolic system MetaMax 3B (Macfarlane & Wong, 2012). Before each investigation metabolic gas analyzer as well as respiratory flow sensors were calibrated according to the manufacturer's instructions. Tri-axial acceleration as well as heart rate and respiration were recorded using a breast belt sensor (Equivital, Hidalgo, GB). The Equivital EQ-01 System is a compact, ambulatory device providing the collection of physiological data like ECG, heart rate, inter beat intervals, breath rate and tri-axial acceleration (Weippert et al., 2013). Data of the EQ-01 recording unit were send via Bluetooth® to a smartphone and further transmitted to a web data base (Rieger et al., 2012). After the experiment data were exported for the statistical analysis. The protocol bases on the tasks identified by observation of operators during routine manual and semi-automated cell culturing process at the Center for Life Science Automation (Rostock, Germany, Table 1). Cardio-respiratory parameters like heart rate (HR), breathing frequency, oxygen uptake (VO_2) – an indicator of energy consumption –, and blood pressure (DBP, SBP) were measured and analyzed during steady state conditions. ANOVA for repeated measures was used to test for significant differences across task conditions, Bonferroni´s correction was applied for post-hoc pair wise comparisons.

Table 2. Anthropometric and physical fitness data of the study participants

	Men (n=10) Median (range)	**Women (N=10) Median (range)**
Age [yrs]	25.0 (22-29)	23.0 (23-27)
Body height [cm]	185.0 (176-190)	170.0 (162-175)
Body weight [kg]	78.0 (62-81)	58.0 (53-62)
Physical Activity Rating (PAR)	8.5 (7-11)	8.0 (5-10)
Perceived Functional Ability 1 (PFA 1)	11.5 (10-13)	9.0 (6-11)
Perceived Functional Ability 2 (PFA 2)	11.0 (8-13)	7 (4-9)
PFA Sum	22.5 (18-26)	16.0 (11-20)
BMI [kg/m²]	22.5 (19.6-24.2)	20.0 (18.9-23.6)
VO_2max (Bradshaw et al. 2005) [ml/min*kg^{-1}]	54.9 (52.5-61.5)	45.3 (41.0-49.8)
VO_2max (Weippert & Stoll 2013) [ml/min*kg^{-1}]	52.3 (47.7-58.6)	43.1 (36.5-48.6)

Figures 2 a-c. Participants during different protocol tasks wearing the mobile respiratory gas analyzer MetaMax 3B (a,b), subject wearing the EQ-01 breast belt monitor

RESULTS

There were strong effects of task condition on blood pressure (SBP: $F(10,210)=30.8$, $p<0.001$, $\eta^2 = .618$; DBP: $F(10,190)=17.9$, $p=.000$, $\eta^2= .485$), HR ($F(10,210)=34.5$, $p<0.001$; $\eta^2= .793$) and VO_2 ($F(10,210)=253.5$, $p<0.001$; $\eta^2= .969$). Figures 3-5 show mean values and standard deviations across the different tasks and significance levels for the post hoc pair wise comparisons with sitting rest.

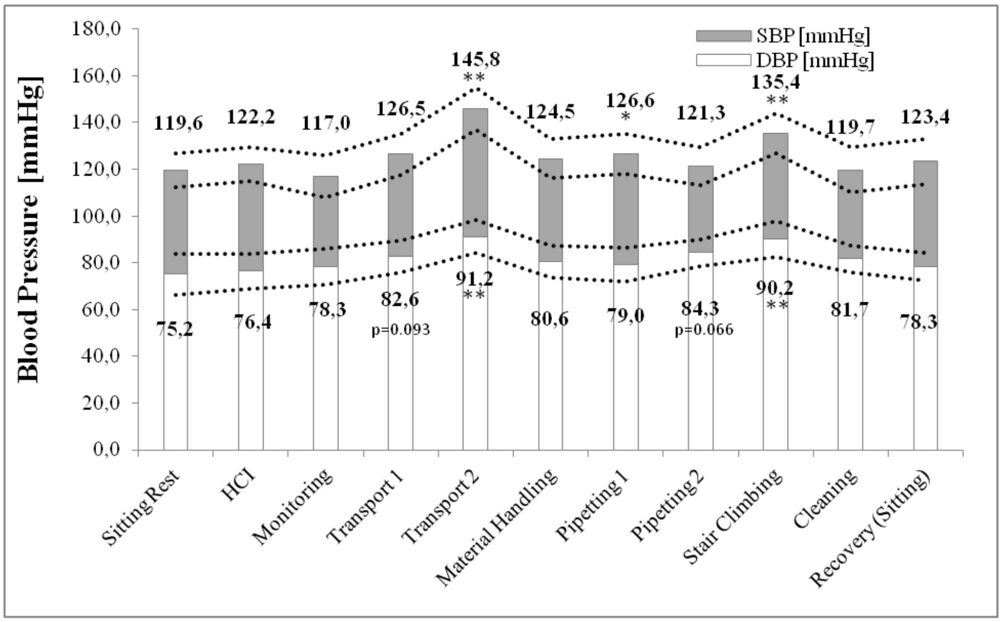


Figure 3. Diastolic and systolic blood pressure response of participants during rest, different laboratory tasks and recovery (N = 20), dotted lines represent Mean±SD; */** significantly different from *Sitting Rest* ($p<0.05$/ $p<0.01$)

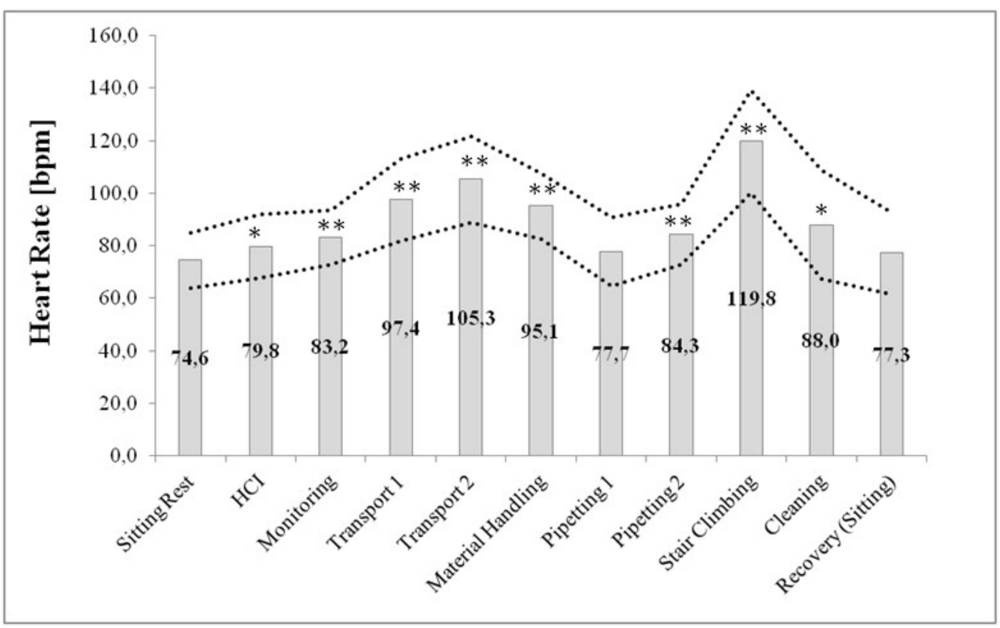


Figure 4. Heart rate response of participants during rest, different laboratory tasks and recovery (N = 20) dotted lines represent Mean±SD; */** significantly different from *Sitting Rest (*p<0.05/ p<0.01)

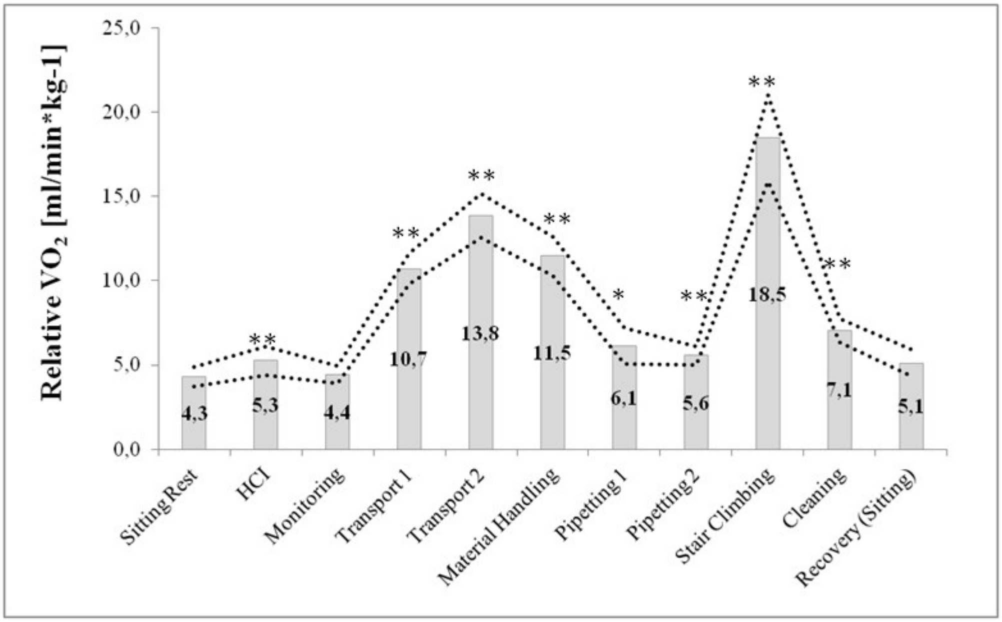


Figure 5: Average oxygen uptake of participants during rest, different laboratory tasks and recovery (N = 20), dotted lines represent Mean±SD; */** significantly different from *Sitting Rest (*p<0.05/ p<0.01)

CONCLUSIONS

Little is known about how typical demands in the field of life science affect blood pressure and other physiological parameters. This study aimed to assess blood pressure, respiratory and cardiac response to typical tasks in life science labs. Ambulatory blood pressure monitoring at regular intervals across a day or during an exercise test reveals only transient values of systemic blood pressure that might not be representative for occupational blood pressure responses. Thus, our experimental study adds physiological information to occupational research in the growing field of biotech workplaces.

Not surprisingly, we found that transportation tasks including larger isometric muscular actions elicited the strongest increase of blood pressure. It is known, that physical (isometric) workload can be associated with an increased risk of elevated blood pressure, which – in turn – is a risk factor for coronary heart disease (Clays et al., 2012; Virkkunen, Harma, Kauppinen, & Tenkanen, 2007). However, as the SBP values do not exceed 210 mmHg and muscular loads occur only intermittent during a work shift of a life science operator these elevations might be uncritical (Mancia et al., 2013). Nevertheless, individual assessment is advised for persons at risk (hypertension, musculoskeletal disorders) as our data mirror the average response of young and healthy volunteers. Further, conclusions have to be drawn cautiously, as there is no consensus on cut-off values for blood pressure during dynamic exercise testing or for intermittent work-related blood-pressure elevations (Mancia et al., 2013). Pipetting in the sitting position elicited a small but significant increase of SBP as well. Pipetting, cleaning and human-computer interaction tasks induced only minor but significant increases of VO_2. Stair climbing elicited the strongest increase in oxygen uptake, followed by material transportation and handling. An 80% increase of heart rate was seen during stair climbing, which corresponded to the large increase in VO_2 during this condition. Nevertheless this increase can be classified as moderate. Summarizing, based on the HR and VO_2-measurements, the intensity of the analyzed tasks, especially when isometric muscular actions can be excluded, can be classified as light to moderate (Grandjean, 1991).

From a preventive perspective the inclusion of physical activity of light to moderate or even intense intensity (dynamic type) into the daily (work) routine can be recommended, especially when having/leading a rather sedentary job/life. Our task analysis and the subsequent experimental study implicate that 1st semi-automation of processes in the life science is not necessarily associated with a reduction in physical activity at work, 2nd the present physical tasks in life science labs can be well tolerated by healthy young operators and 3rd may help to limit the negative consequences of a sedentary life style when reaching sufficient duration and frequencies (Löllgen, Völker, Böckenhoff, & Löllgen, 2006).

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REFERENCES

Clays, E., De Bacquer, D., Van Herck, K., De Backer, G., Kittel, F., & Holtermann, A. (2012). Occupational and leisure time physical activity in contrasting relation to ambulatory blood pressure. *Bmc Public Health, 12*, 1002. doi: 10.1186/1471-2458-12-1002

Grandjean, E. (1991). *Physiologische Arbeitsgestaltung - Leitfaden der Ergonomie*. Landsberg: ecomed.

Löllgen, H., Völker, K., Böckenhoff, A., & Löllgen, D. (2006). Physical activity and prevention of cardiovascular diseases. Körperliche Aktivität und Primärprävention kardiovaskulärer Herzkrankungen. *Herz, 31*(6), 519-523.

Macfarlane, D. J., & Wong, P. (2012). Validity, reliability and stability of the portable Cortex Metamax 3B gas analysis system. *European journal of applied physiology, 112*(7), 2539-2547. doi: 10.1007/s00421-011-2230-7

Mancia, G., Fagard, R., Narkiewicz, K., Redon, J., Zanchetti, A., Bohm, M., . . . Task Force, M. (2013). 2013 ESH/ESC Guidelines for the management of arterial hypertension: the Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *Journal of hypertension, 31*(7), 1281-1357. doi: 10.1097/01.hjh.0000431740.32696.cc

Rieger, A., Neubert, S., Behrendt, S., Weippert, M., Kreuzfeld, S., & Stoll, R. (2012, 20-23 March). *24-Hour ambulatory monitoring of complex physiological parameters with a wireless health system: Feasibility, user compliance and application.* Paper presented at the 9th International Multi-Conference on Systems, Signals and Devices (SSD), Dresden (Germany).

Virkkunen, H., Harma, M., Kauppinen, T., & Tenkanen, L. (2007). Shift work, occupational noise and physical workload with ensuing development of blood pressure and their joint effect on the risk of coronary heart disease. *Scandinavian journal of work, environment & health, 33*(6), 425-434.

Weippert, M., Stielow, J., Kumar, M., Kreuzfeld, S., Rieger, A., & Stoll, R. (2013). Tri-axial high-resolution acceleration for oxygen uptake estimation: Validation of a multi-sensor device and a novel analysis method. *Applied Physiology, Nutrition, and Metabolism, 38*(3), 345-351.